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09/393,441	09/08/99	ANDERSON C	660088.420C1

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EXAMINER	
SCHNIZER, H	
ART UNIT	**PAPER NUMBER**
1653	10

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

FILE COPY

Office Action Summary	Application No. 09/393,441	Applicant(s) ANDERSON ET AL.	
	Examiner Holly Schnizer	Art Unit 1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *15 February 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42, 43, and 46-57* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42, 43, and 46-57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5 and 7* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

Status of the Claims

1. The Response to the Restriction Requirement filed February 15, 2001 (Paper No. 9) has been entered. Claims 1-41, 44-45, and 58-112 have been canceled. Therefore, Claims 42, 43, and 46-57 are pending and will be examined on the merits in this Office Action.

Election/Restriction

2. Applicant's election of Group 6, Claims 42, 43, and 47-57 in Paper No. 9 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Drawings

3. The drawings have been objected to for defects noted on the Form PTO-948. Correction is required.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 42 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claim 42 is indefinite for depending from canceled claims. Correction is required.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 42, 43, and 46-57 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

9. Applicant is referred to the interim guidelines on written description published December 21, 1999 in the Federal Register, Volume 64, Number 244, pp. 71427-71440 (available at www.uspto.gov) and the Examiner training Materials on Written Description also available at www.uspto.gov.

10. Claims 42, 43, and 47-57 are genus claims. Claims 42 is directed the genus of any adenine nucleotide translocator (ANT) protein. Claims 43 and 47-51 are drawn to the genus of any human ANT proteins or human ANT fusion proteins, Claims 52-57 are drawn to the genus of any animal ANT proteins, and Claim 46 is drawn to any ANT3 polypeptide or variant or fragment thereof.

11. The specification indicates that an ANT variant is a polynucleotide that encodes an analog having an insertion, deletion, or substitution (p. 21, entire page, especially lines 18-25) and a "fragment" as any ANT polypeptide that retains "essentially the same biological function or activity" as an ANT polypeptide (p. 23, lines 3-6). The specification and claim do not place any limit on the number of amino acid substitutions, deletions, and/or additions that may be made. Therefore, the scope of the claim

includes variants and fragments of any length and sequence. The genus is highly variant because a significant number of structural differences between genus members is permitted and the specification and claims do not indicate what distinguishing attributes are shared by the members of such a genus (see Examiner's Training Materials on Written Description, Example 13). The specification does not define when a protein ceases to be an ANT3 polypeptide or even when a protein ceases to be any ANT polypeptide. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is extremely variant, then the three species, ANT 1, ANT 2, and ANT3 having the sequences defined by SEQ ID Nos: 31-33 alone are insufficient to describe the genus of any ANT protein having any sequence and any length. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, the disclosure is insufficient to show that one of skill in the art would conclude that applicant was in possession of the claimed genus.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

13. Claims 42, 43, and 46 rejected under 35 U.S.C. 102(a) as being anticipated by Marzo et al.(Science (Sept. 25, 1998) 281(5385): 2027-2031; ref. CC in IDS filed Sept. 8, 2000 as Paper No. 5).

14. Marzo et al.disclose a purified human ANT2 protein (p. 2029, Col. 1, lines 9-32, Fig. 2C, Fig. 4). Marzo et al. state that ANT was purified to greater than 95% homogeneity and found to be uncontaminated by other proteins (see p. 2029, Col. 1, lines 29-31). ANT2 is considered a variant of ANT3. Therefore, Marzo et al. meets the limitations of Claims ~~42-46~~ 42, 43, and 46.

15. Claims 42, 43, and 46 are rejected under 35 U.S.C. 102(a) as being anticipated by Fiore et al. (Biochimie (Feb. 1998) 80: 137-150; ref. BE of IDS filed Sept. 8, 2000 as Paper No. 5).

16. Fiore et al. provide a review of mitochondrial ADP/ATP carrier proteins (also known as ANT proteins) and provides evidence that ANT proteins are very well known in the art. Figure1 of the Fiore et al. reference provides an amino acid sequence alignment of known ANT proteins from human, bovine, mouse, rat, as well as other sources. In particular, the sequences of human ANT 1, 2 and 3 are provided. The Fiore et al. reference indicates that the ANT proteins from human and animal sources have not only been isolated but are also fairly well characterized. For example, Fiore et al. state "the definite characterization of the ADP/ATP carrier as a transport protein was established after reincorporation of the isolated carrier into liposomes and reconstitution of transport" (p. 138, Col. 1, last 4 lines of the column) and the beef heart ADP/ATP

carrier isolated in the presence of detergent is able to undergo the transition between two conformational states (pl. 145, Col. 1, lines 1-9).

Claim Rejections - 35 USC § 103

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

19. Claims 42, 43, 46-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fiore et al. (Biochimie (Feb. 1998) 80: 137-150; ref. BE of IDS filed Sept. 8, 2000 as Paper No. 5) in view of Rosenberg (Protein Analysis and Purification: Benchtop Techniques (1996) Birkhauser, Boston, pages 335-347; ref. CE of IDS filed Sept., 8, 2000 as Paper No. 5).

20. The teachings of Fiore et al. have been described above. Fiore et al. also disclose that a yeast strain containing an ANT carrying a polyhistidine tag at the C terminus was constructed to allow purification by immobilized metal ion affinity chromatography (p. 144, Col. 1, last paragraph). However, Fiore et al. do not teach a human or animal ANT fusion protein.

21. Rosenberg shows that it is standard in the art to construct fusions between a protein of interest and an enzyme (for example, β-galactosidase (β-Gal) (p. 336, lines 3-6 and section titled "Expression and Purification of lacZ and trpE Fusion Proteins") or an affinity tag (for example His-Tag or FLAG or GST (see p. 341-347)). Rosenberg teaches that using β-Gal as the fusion partner provides an advantage because antibodies to β-Gal can be used to affinity purify the fusion protein and to follow purification of the fusion protein by Western blot analysis of the various fractions. Rosenberg also teaches that a protease cleavage site can easily be engineered into the fusion so that the fusion partner can be separated from the protein of interest after purification (see p. 344, Section 11.15).

22. Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to express the well known human and animal ANT protein sequences taught in Fiore et al. as fusion proteins wherein the fusion partner was a polypeptide or enzyme having affinity for a ligand. One would have been motivated to do so because such a protein would allow easier purification on an affinity column. Using β-Gal as the fusion partner has the added benefit that the fusion protein can be easily monitored during purification (for optimization of purification conditions) or during

expression (to localize the fusion protein in cells using the enzymatic activity of the β-Gal protein).

23. Claims 42, 43, 50, 52-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Adrian et al. (Mol. Cell Biol. (1986) 6(2): 626-634) in view of Fiore et al. (. (Biochimie (Feb. 1998) 80: 137-150; ref. BE of IDS filed Sept. 8, 2000 as Paper No. 5).

24. Adrian et al. disclose the expression of fusion proteins comprising *Saccharomyces cerevisiae* ADP/ATP translocator (ANT) proteins of various lengths (see p. 631, Fig. 5) and the enzyme β-Galactosidase in an investigation of what amino acids are important in targeting the protein to the mitochondrial membrane. The study reveals that several of the fusion proteins were delivered to the mitochondria (see p. 630, Col. 2, lines 23-30; and p. 631, Table 1).

25. Adrian et al. do not teach that the ANT proteins were derived from human or animal sources.

26. As described above, Fiore et al. disclose the amino acid sequence alignment of 29 sequences of known ANT proteins from human and animal sources, and indicate that these proteins have been isolated (p. 145, Col. 1, lines 1-9).

27. Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to express the human and animal ANT proteins described in Fiore et al. as fusion proteins as taught in Adrian et al. One having ordinary skill in the art would have been motivated to substitute human or animal ANT instead of the disclosed

yeast ANT in order to study the mitochondrial localization sequences in human and animal ANT. Characterization of animal and more importantly human ANT proteins is essential to the development of diagnostic and treatment tools because as taught in Fiore et al. (p. 146, Col. 2), these proteins have a central role in cellular energy metabolism and it is likely that dysfunction of these proteins is involved in mitochondrial disorders.

28. Additional References

29. Brandolin et al. (Biochemistry (1985) 24: 1991-1997), referenced in Fiore et al. above (reference number 48 , cited on page 145, Col. 1, first paragraph), provides another example that adenine nucleotide translocators from animals were very well known in the art at the time of the invention and that these proteins could be isolated and purified successfully. The Brandolin et al. reference describes the isolation and purification of an adenine nucleotide carrier protein (also known as adenine nucleotide translocator, see Fiore et al.) from beef heart mitochondria.

Double Patenting

30. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in

scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

31. Claims 42, 43, and 46-57 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 42, 43, 46-57 of copending Application No. 09/185,904. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Conclusion

32. No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Holly Schnizer whose telephone number is (703) 305-3722. The examiner can normally be reached on Mon. & Thurs., 8am-5:30pm and Tues. & Wed. 9-2:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (703) 306-4119. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703 308-0196.

Karen Cochrane Carlson PhD

KAREN COCHRANE CARLSON, PH.D
PRIMARY EXAMINER

HS
April 30, 2001